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Amniotic Fluid Embolism and the Possible Protective Effects of Heterozygous Factor V Leiden: A Case Report

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Introduction

Amniotic fluid embolism (AFE) is a rare and commonly fatal [1-3] obstetric emergency theorized to trigger an inflammatory reaction much like the systemic inflammatory response syndrome (SIRS) of sepsis [4,5], leading to vascular constriction and coagulation. This often results in ARDS, cardiac arrest, disseminated intravascular coagulation (DIC), and death [6]. With such similar theorized mechanisms, we suspect factors that may modify mortality in sepsis may also modify mortality in AFE. Specifically, we ask if alterations in the coagulation cascade of heterozygous Factor V Leiden mutation (FVL+/-) can decrease mortality in AFE, as seen in studies with severe sepsis [7,8]. The following case describes the labor course of a patient with FVL+/- complicated by a postpartum AFE that did not progress to DIC.

Table 1: Diagnostic criteria for AFE

1. Sudden onset of cardiorespiratory arrest, or both hypotension (systolic blood pressure <90 mm Hg) and respiratory compromise (dyspnea, cyanosis, or peripheral capillary oxygen saturation [SpO2] <90%)
2. DIC*
3. Clinical onset during labor or within 30 min of delivery of placenta
4. No fever (≥38.0°C) during labor

*per Scientific and Standardization Committee on DIC of the International Society on Thrombosis and Haemostasis (ISTH) scoring system

Case

Patient is a 31-year-old G2P0 with a history of FVL$^{+/-}$ that presented for a scheduled induction of labor at 40 weeks and 5 days gestational age. During her induction, an umbilical cord prolapse required an emergent cesarean section. She suddenly developed shortness of breath, confusion, cyanosis, hypotension, bradycardia, and hypoxemia, with a sharp decline in oxygen saturation, from 92% to 21% approximately 30 minutes after. She lost radial/carotid pulses, CPR was initiated, and she was intubated. Pulses returned after 3 rounds of chest compressions and a dose of epinephrine. She was transferred to the ICU where she was started on Levophed for refractory hypotension. EKG showed sinus bradycardia. Chest X-ray showed severe airway disease (Figure 1A). Chest CTA further demonstrated airspace opacities in both lungs (Figure 2). There was no evidence of DVT. Other lab findings showed hypokalemia, lactic acidosis, normal coagulation panel, and a fibrinogen level of 399 mg/dL. The patient's condition drastically improved overnight, and she was successfully extubated the next day. Repeat chest X-ray showed significant improvement (Figure 1B). Patient was transferred to mother-baby the following day, started on therapeutic Lovenox, and discharged home on post-operative day 5.

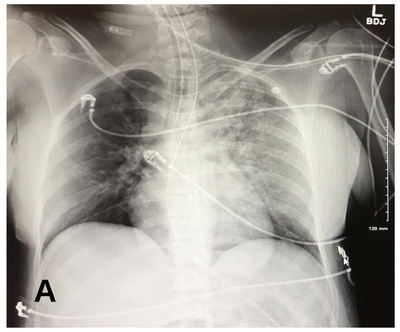

Figure 1: A. Opacity and consolidation of almost the entire left lung. Mild venous congestion noted. B. Significant improvement of the now mild bilateral airspace disease the following day,

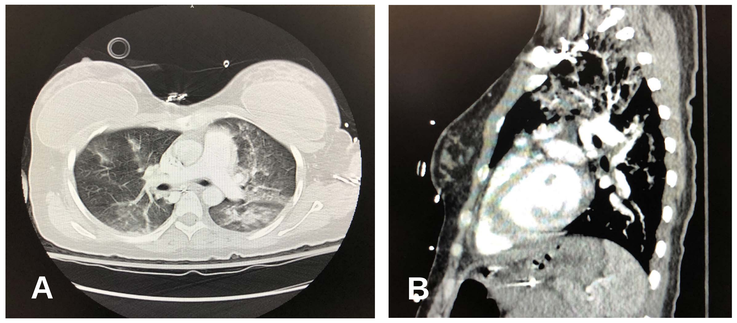

Figure 2: Multiple CT angiogram views of the chest showing severe airspace opacities of the left lung and moderately severe airspace opacities of the right lung suggestive of amniotic fluid embolism. No evidence of right ventricular prominence or strain pattern. A. Transverse view B. Sagittal view

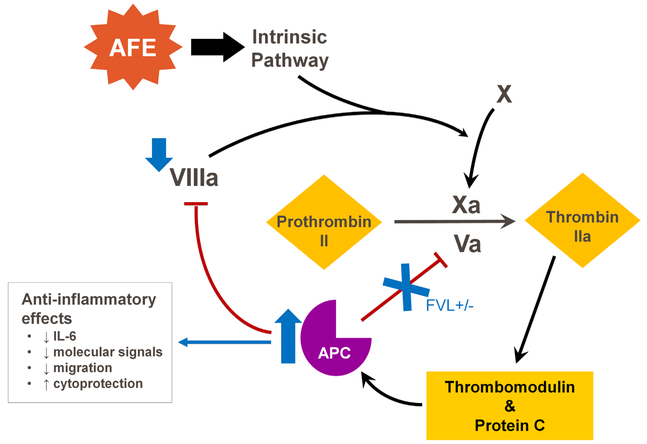

Figure 3: Thrombin converts factor V to the activated form, factor Va. A complex of thrombin with the endothelial cell receptor thrombomodulin activates protein C (APC) which inactivates factor Va and VIIIa. We suggest that the APC resistance in heterozygous Factor V Leiden mutation (FVL+/-) leads to shunting of APC towards the anti-inflammatory pathway, and may blunt the procoagulant and inflammatory effects of AFE and subsequent development of DIC.

Discussion

With DIC being one of the criteria set by the Society for Maternal-Fetal Medicine (SMFM) and Amniotic Fluid Embolism Foundation (Table 1) for AFE diagnosis, we present an atypical presentation of AFE due to the absence of DIC. Defined by uncontrolled microvascular thrombosis and coagulation factor depletion, DIC has been associated with increased mortality rates in the setting of severe sepsis [9]. As DIC does not always present with sepsis or AFE, it appears there may be certain mechanisms that alter the coagulation cascade, and thus, the risk of developing DIC. One would believe that FVL$^{+/-}$ would lead to increased mortality in the setting of sepsis. However, the opposite has proven to be true [8]. In FVL$^{+/-}$, Factor V is resistant to cleavage by activated Protein C (APC), leading to increased thrombin and a hypercoagulable state. It is known that hypercoagulability activates the thrombomodulin/APC mechanisms [7,10]. These mechanisms increase the anti-inflammatory processes believed to attenuate DIC, which become severely impaired in sepsis [10] (Figure 3). It is reasonable to believe that the increased availability of APC along the anti-inflammatory pathways explains why our patient did not progress to overt DIC and ultimately survived this event. Finally, is there a way to utilize this pathway to improve survival rates in other AFE cases or in severe sepsis?

Conclusion

Whether FVL$^{+/-}$ is an evolutionary advantage given the high prevalence in the population versus an unfavorable inheritance remains controversial. It seems the largest protection of FVL$^{+/-}$ lies behind its mechanism to decrease mortality in severe sepsis and DIC development, protecting pregnant patients against one of the most fatal complications: Amniotic Fluid Embolism. Whether this was just an atypical AFE presentation or a protective effect of FVL$^{+/-}$ is unknown due to the lack of similar published cases, retrospective or prospective studies. More research is required to fully understand the role of FVL$^{+/-}$ and APC resistance in the potential prevention of DIC or sepsis associated coagulopathy.

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