

Anaphylactoid Syndrome of Pregnancy—An Autopsy Case Report

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Case Report

A young woman presented for induction of labor secondary to insulin-dependent gestational diabetes. The patient went into spontaneous cardiac arrest shortly after rupture of the membranes, and the infant was subsequently delivered via emergency cesarean section. The documented clinical impression included disseminated intravascular coagulation secondary to presumed amniotic

fluid embolism. Despite cardiopulmonary resuscitative efforts, the mother was pronounced deceased.

A complete autopsy was performed. The external examination was without significant findings. On internal examination, the lungs were congested and edematous (the right lung weighed 740 grams, and the left lung weighed 600 grams). The heart weighed 320 grams and was without evidence of coronary artery dissection, cardiomyopathy, ischemic injury, or other abnormality. The brain was free of hemorrhage, and the remainder of the internal examination was noncontributory. Microscopic examination demonstrated diffuse pulmonary vascular congestion and alveolar extravasations of red blood cells. There was a bilateral presence of

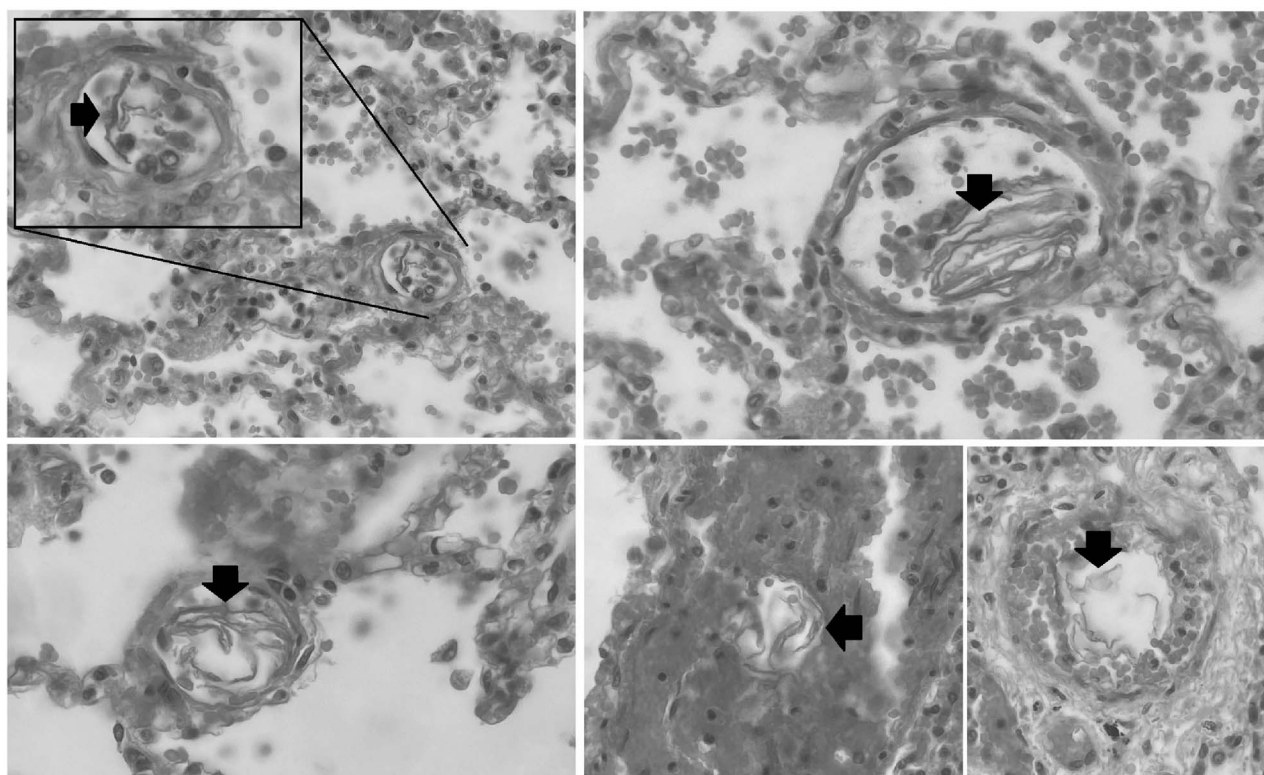


FIGURE 1. Present in small- and medium-sized pulmonary vessels were aggregates of fetal squames (arrows).

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squamoid particles in both small- and medium-sized vessels, consistent with fetal squames (Fig. 1). Also present were numerous platelet thrombi, with the occasional commingled presence of platelet thrombi and adjacent fetal squames (Fig. 2). An Alcian blue–stained section showed the presence of intravascular mucin (Fig. 3). The autopsy findings were confirmatory of the clinical impression of amniotic fluid embolism.

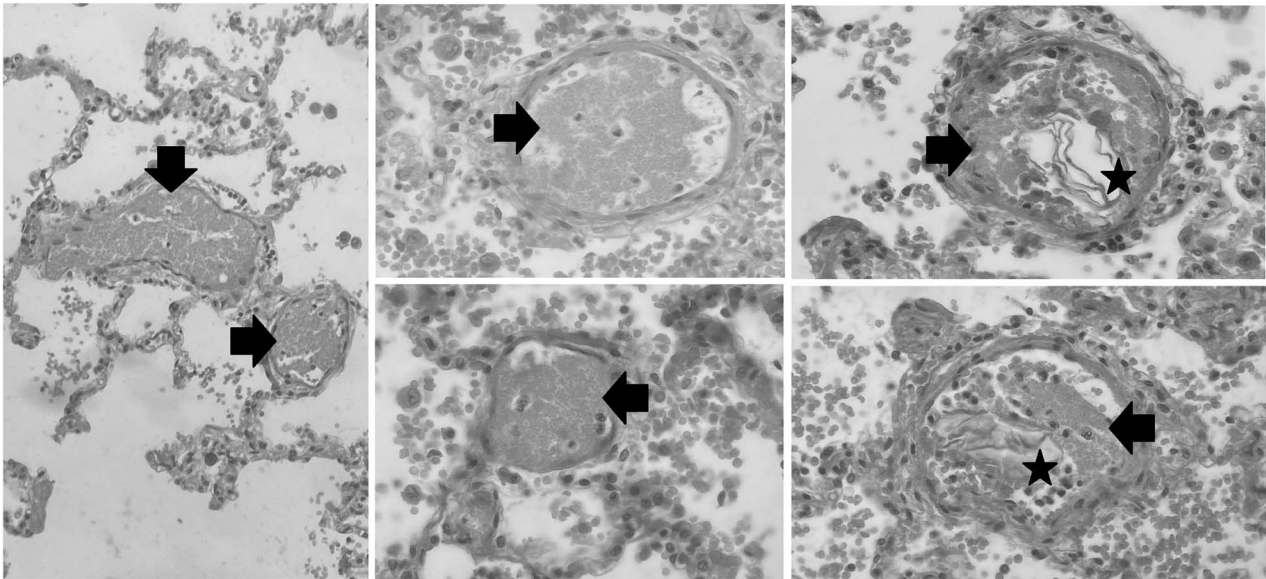


FIGURE 2. Also present in small- and medium-sized pulmonary vessels were platelet thrombi (arrows), to include the comingled presence of adjacent fetal squames (stars).

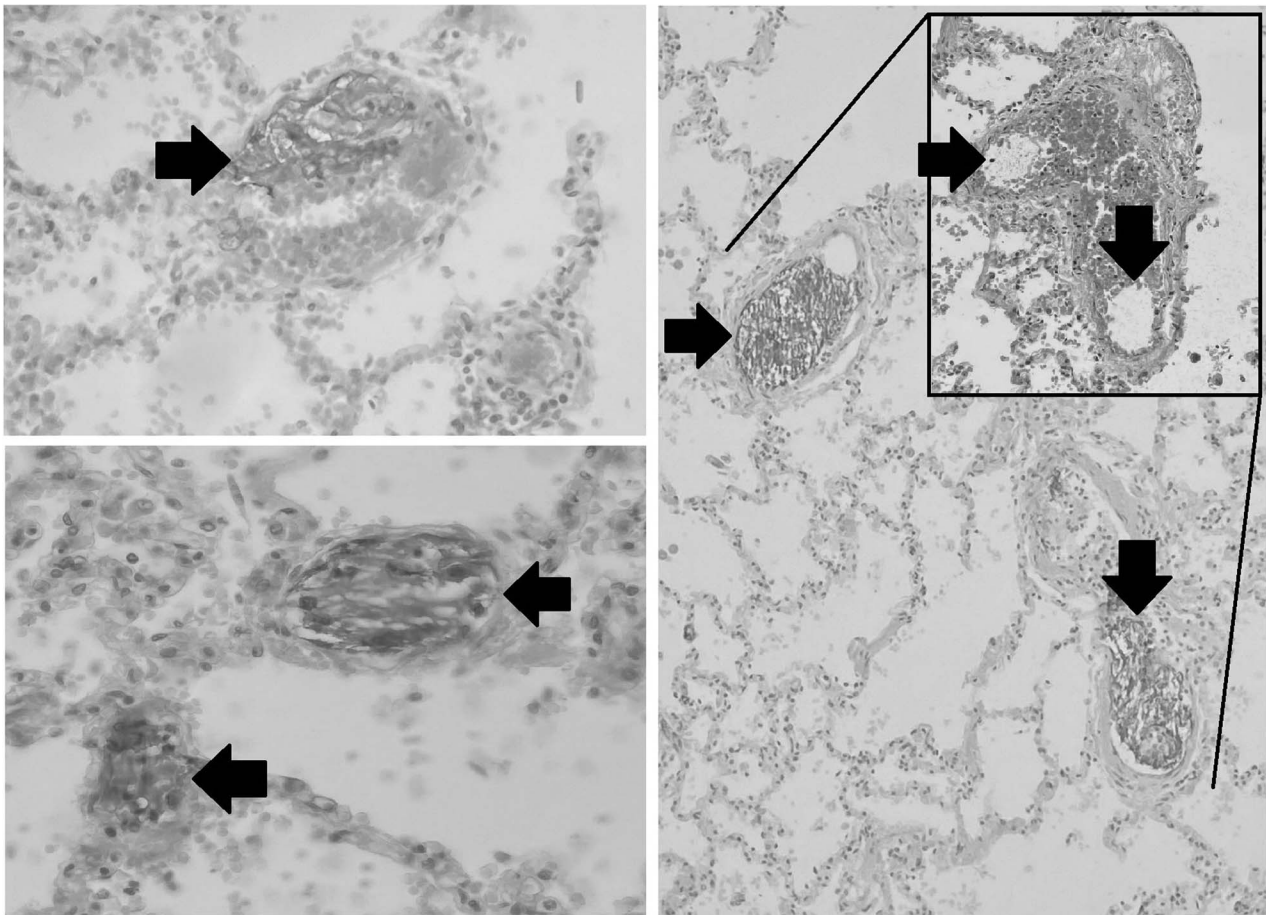


FIGURE 3. An Alcian blue stain highlighted the presence of intravascular mucin (arrows); insert provides corresponding hematoxylin and eosin stain for comparison.

DISCUSSION

Anaphylactoid syndrome of pregnancy (ASP)—previously referred to as amniotic fluid embolism—is a rare and devastating complication of pregnancy, with both poor maternal and fetal outcomes. The annual incidence is 5.1% per 100,000 deliveries,¹ causative of permanent neurologic injury, or death in approximately 85% of women and neurologic injury in 50% of neonates with a mortality rate of 21%.^{2–4} The most prevalent risk factor is maternal age older than 35 years,⁵ although eclampsia, diabetes, amniocentesis, and placenta previa and placental abruption have all been reported as risk factors.⁶ One of the few modifiable risk factors include induction of labor with the use of uterotonics increasing the incidence, which was strongly associated with fatalities,⁵ as in this case.

Although the exact pathophysiology of ASP is unclear, the inciting event is the introduction of amniotic fluid into the maternal circulation. This can not only occur in different ways, including amniotomy, but can also occur via tears in the uterus or cervix via vaginal delivery or during cesarean delivery; the 3 proposed sites of entry are endocervical veins, uterine trauma sites, and the placental attachment site.^{2,7,8} Once introduced, amniotic fluid makes its way into the maternal pulmonary circulation. Subsequent proposed responses include either (1) a reaction secondary to the obstruction of pulmonary blood flow or (2) a proinflammatory reaction secondary to the release of cytokines derived from arachidonic acid from the amniotic fluid, resulting in an anaphylactoid reaction.^{2,9} Regardless of the mechanism, the resultant pulmonary edema and corresponding pulmonary hypertension result in acute respiratory distress syndrome, hypotension, and hypoxia.¹⁰

Estimates of maternal mortality rates from ASP range from 24% to 80%.¹ The leading cause of death in 80% of cases of ASP is cardiac arrest secondary to heart failure.^{3,9} Due to lack of oxygenation secondary to cardiac arrest, both maternal and fetal neurologic deficits can occur. Up to 45% of cases develop disseminated intravascular coagulation within 30 minutes to 4 hours after the inciting event, secondary to the activation of excessive fibrinolytic activity due to procoagulant components in the amniotic fluid.¹¹ This results in massive and uncontrollable hemorrhage, metabolic acidosis, multiorgan system failure, and maternal death. As many as 85% of survivors have permanent neurologic injury due to hypoxia.^{2,4} Because of concordant uterine atony due to increase in fibrin split products, many women undergo hysterectomy and resultant loss of fertility.¹¹ In terms of neonatal outcomes, fetuses can have such severe hypoxemia that they are stillborn or have permanent neurologic injury.^{3,6}

Diagnosis of ASP involves early recognition of clinical signs. The 4 identified cardinal signs of ASP, which can occur in any order, and up to 48 hours after birth, include hypoxia, altered mental status, hypotension with shock, and disseminated intravascular coagulation.² Despite the diagnostic criteria, the diagnosis is largely one of exclusions. Currently, there is development of a biomarker to detect amniotic fluid that has passed into circulation.¹² Definitive diagnosis has routinely required postmortem confirmation of the

histologic presence of fetal debris within the maternal pulmonary vasculature, although it should be noted that the presence of fetal cells within the maternal vasculature is not by itself pathognomonic for ASP.¹ Pathologic confirmation of ASP can be aided by the use of cytokeratin immunostains (ie, AE1/AE3), a Zn-Cp1-stain that highlights meconium, or an Alcian blue stain to highlight mucin, a component of amniotic fluid.¹ Also reported is the use of a CD88 immunostain (C5a receptor) to demonstrate complement activation.¹

In the present case, the confirmation of mucin by an Alcian blue stain along with the presence of squames and platelet thrombi in the maternal pulmonary vasculature was consistent with the clinical impression of ASP. As such, confirmatory immunostains were not regarded as necessary. Although these deaths commonly occur in hospital settings, they may also occur after home births, and therefore, forensic pathologists need to be familiar with this entity and its diagnosis.

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