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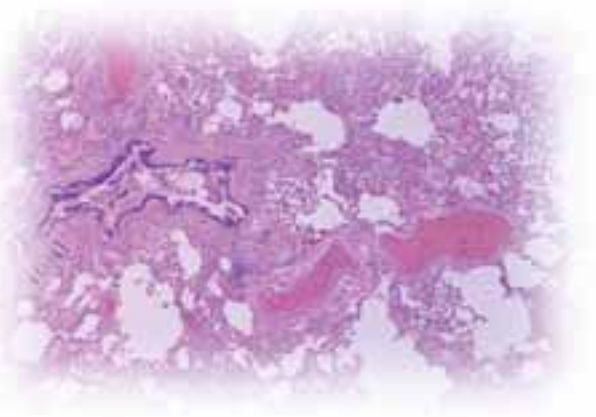
Managing amniotic fluid embolism

The rarity of AFE and the fact that presentation is acute make it difficult to establish an optimal therapy. An expert reviews findings from selected series and offers guidelines on managing this life-threatening collapse.

Amniotic fluid embolism (AFE) is a dramatic and perplexing condition. Within moments of the appearance of symptoms, a gravida's life is at stake, and both maternal and fetal deterioration are rapid. Further, because the diagnosis isn't always clear, the hospital team must rule out other possible etiologies while trying to prevent respiratory arrest and hemorrhage. The relative rarity of AFE adds to the difficulty of deciphering its pathophysiology. That rarity, coupled with the complexity of management, may explain why AFE remains a leading cause of maternal death. In the United Kingdom over the past 15 years, AFE has been responsible for 8.4% of maternal deaths. In the United States and Australia, it has been associated with 7.5% to 10% of these deaths.[1-3]

Fortunately, a gloomy prognosis may no longer be inevitable. Over the past 20 years or so, mortality rates for AFE appear to have dropped. Still, when this condition presents, immediate action is vital if there's any hope of saving mother and fetus. Here, I present clinical features that may signal an AFE and describe various management strategies outlined in the literature.



KEY POINTS

- Amniotic fluid embolism is a leading cause of maternal mortality in developed countries.
- It presents with maternal collapse or seizures, or occasionally fetal distress.
- Resuscitation must be prompt and multidisciplinary, including delivery if necessary.
- There is no specific therapy except intensive support with transfusion.
- Mortality may not be as high as previously thought, since milder cases do occur.

Declining mortality rates

A 1979 review suggested a mortality rate of 86% for women suffering an AFE. But in a retrospective look at the 1995 US National Amniotic Fluid Embolus Registry, researchers noted a mortality rate of 61%[4,5] (though only 7% to 15% of all the women survived neurologically intact[5]). Other recent surveys report

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TABLE

Amniotic fluid embolism-related mortality and morbidity: selected series

SERIES	SITE	YEAR	NUMBER OF CASES	MORTALITY	OTHER MORBIDITY	INFANTS*
US registry (Clark)[5]	United States	Published 1995 (1988-1993)	46	61%	Only 15% neurologically intact	22/28 survived, 11 (50%) neurologically intact
Burrows and Khoo[3]	Brisbane, Australia	Published 1995 (1984-1993)	9	22%	2/9 had hysterectomy; 1 long-term disability	8/11 survived (2 sets of twins)
Gilbert and Danielsen[6]	California	Published 1999 (1994-1995)	57	28%	5/39 survivors needed "extra arrangements" on discharge†	95% survived; 72% normal discharge
UK registry (D.J.T., unpublished data)	United Kingdom	1997-2000	25	16%	4/21 survivors and 1 of 4 women who died had hysterectomy; 1 surviving woman had internal iliac ligation and liver hematoma; 2 women had renal failure and recovered; 1 woman had subglottic stenosis	3 perinatal deaths; 5/15 survivors severely acidotic

*From cases occurring before or at delivery only.

†The authors did not specify what these "extra arrangements" were.

even lower mortality rates: under 30% (**TABLE**).[3-6]

The changing mortality rate is probably a result of 2 factors: better intensive care and a recognition that "milder" cases do occur. For example, as Benson notes, "the mere fact of survival" was generally considered "proof that a given individual did not have an amniotic fluid embolism."[7] Benson proposes a new clinical definition of AFE that would apply "to patients who survive as well as to those who die."[7] Milder cases tend to present with less dramatic collapse and often only transient hemodynamic change, whereas severe cases are characterized by collapse with cardiac arrest.

Clinical features

The pathophysiology of AFE is poorly understood. Amniotic fluid and fetal cells enter the maternal circulation, leading to sudden maternal or fetal deterioration—the hallmark clinical features of AFE.

In the United States, Clark established clinical criteria for AFE for the national reg-

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istry; these criteria have been followed in the UK since 1997 in an effort to develop a registry of cases there.[5,8] The criteria are:

- acute hypotension or cardiac arrest
- acute hypoxia (dyspnea, cyanosis, or respiratory arrest)
- coagulopathy (laboratory evidence of intravascular coagulation or severe hemorrhage)
- onset of all of the above during labor or within 30 minutes of delivery
- no other clinical conditions or potential explanations for the symptoms and signs

Typically, AFE presents with a cluster of features. This becomes clear when a larger series of cases is considered. In early series reporting a high mortality rate, such as the Morgan series, almost all women presented with cardiorespiratory collapse.[4] Other signs and symptoms were breathlessness, hypotension, collapse (e.g., hypovolemic), and seizures. Fetal signs and symptoms did not figure in the Morgan series, but in 17% of the US series the abnormal fetal-heart-rate (FHR) pattern was bradycardia.[5] In the UK series, 9 cases (36%) presented with abnormal FHR patterns, though not all had bradycardia (D.J.T., unpublished data). Coagulopathy and bleeding were uncommon presenting features in all 3 series, occurring at a rate of 12% in Morgan's series, 0% in the US series, and 4% in the UK series. Coagulopathy and massive hemorrhage seem to be features that develop later. Often the coagulopathy is present shortly after presentation—and can be detected if looked for—but becomes clinically apparent only with time.

The multiple clinical presentations support the hypothesis that the early deaths are caused by the direct and "toxic" effects of a bolus of fetal material or amniotic fluid; the women who survive that initial event then become exposed to the cascade of related problems that follow. Most deaths now occur in this acute phase of collapse.[1]

Older women (i.e., over 25 years of age) appear to be at highest risk. In the past 15 years, only 1 woman under 25 has died of AFE in the UK, and only 2 women under 25 have been reported to the UK national registry.[1] In a nonspecific way, intervention or complications at any stage of pregnancy seem more common in women who go on to have an AFE, though no distinct trigger has been found. Multiparity has been suggested as a risk factor, but neither the UK nor US registries have corroborated this.[5] Eight of the 25 women reported to the UK registry were primiparas, and 1 had experienced 2 miscarriages but no other pregnancies. While labor is important in the etiology of AFE, cases have been reported under other circumstances, particularly after cesarean section, blunt abdominal trauma, amniocentesis, a ruptured uterus, and amnioinfusion in labor.[9-13]

The most useful diagnostic test to rule out a large segment of the differential diagnosis is a clotting screen.

Differential diagnosis

The diagnosis of AFE is often one of exclusion—or else it is made postmortem. The differential diagnosis includes an exhaustive list of the causes of maternal collapse in the peripartum period. These include thrombotic embolus, air embolus, septic shock, acute myocardial infarction, peripartum cardiomyopathy, anaphylaxis, aspiration, placental abruption, transfusion reactions, local anesthetic toxicity, preeclampsia or eclampsia, uterine rupture, and postpartum hemorrhage (uterine atony).[8,12]

Management

Initial management is supportive rather than specific. Basic resuscitation must be started immediately. Maximal initial oxygenation is required and, usually, early intubation and ventilation. An important step to consider is

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prompt delivery by cesarean section if the woman does not respond to cardiopulmonary resuscitation after 5 minutes. Prompt transfusion of fluids is necessary to replace blood loss. Vasopressors such as phenylephrine may help restore aortic perfusion pressure.[12]

As with any collapse, the early involvement of senior, experienced staff is critical, since the technical and practical aspects of resuscitation are more likely to be expertly performed by people who practice them regularly. A multidisciplinary approach—involving obstetricians, anesthesiologists, intensivists, and hematologists—carries the best prospect of the woman's survival.

While the patient is being resuscitated, the team will have to investigate other causes of the collapse. The most useful diagnostic test to rule out a large segment of the differential diagnosis is a clotting screen. Clotting is often extremely abnormal even before the hemorrhage becomes apparent. If the patient is already hemorrhaging, abnormal clotting secondary to the hemorrhage needs to be considered. However, hemorrhage will not usually by itself cause a coagulopathy, unless there is considerable blood loss and blood replacement.

Because there is some "toxic" element to the effects of amniotic fluid, a number of reports have suggested that hemofiltration or plasma exchange may be effective.

If there are any signs of coagulopathy, such as blood in the urine or bleeding from the gums, the team should consider replacing clotting factor with fresh frozen plasma, cryoprecipitate, and platelets—even before massive blood loss is apparent and certainly before receiving the laboratory confirmation of coagulopathy. Indeed, cryoprecipitate may be of intrinsic value beyond its clotting-factor components because it contains fibronectin,

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which helps the reticuloendothelial system filter antigenic and toxic particulates.[12]

It also is important to perform an electrocardiogram to look for signs of myocardial damage. Be aware, however, that AFE can cause bizarre cardiac rhythms, which may need specific treatment and can make interpretation difficult. Because myocardial suppression is more common, dopamine or other inotropes may be helpful. Early pulmonary-artery catheterization is recommended to guide therapy.[3,8,12] In fact, this step may be vital, helping prevent fluid overload that can worsen pulmonary edema and lead to adult respiratory distress syndrome. Arterial blood gases also may be of value, in addition to pulse oximetry, but will not differentiate causes specifically. In a patient who becomes stable, a ventilation-perfusion scan of the lungs may demonstrate defects. However, AFE can occlude the pulmonary vessels, so defects do not exclude it as a diagnosis.

If the fetal condition deteriorates suddenly, the team should consider coagulation studies and pulse oximetry. These will be more appropriate if the fetus is unexpectedly severely acidotic. Abnormalities detected by these investigations warrant earlier invasive monitoring, which may improve outcome.

Specific treatments

It is impractical to investigate therapies for AFE in a structured way, as can be done with other conditions. Therefore, management is based on the amalgamated results from other individual cases.

A number of therapies have been used in managing AFE. In 1 case, an AFE was thought to be in progress, as air bubbles and vernix were seen in the left uterine vein at cesarean section.[14] The infundibulopelvic ligament and uterine arteries were ligated and an area of Couvelaire uterus oversewn. Mild coagulopathy occurred, but there were no other problems.

Various techniques of supporting the cardiorespiratory functions have been used in

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the acute phase of the condition. Cardiopulmonary bypass and open pulmonary artery thromboembolectomy produced a good outcome in 1 case.[15] Extracorporeal membrane oxygenation and intra-aortic balloon counterpulsation have also been used successfully.[16] Inhaled prostacyclin has been used to dilate pulmonary vessels, and inhaled nitric oxide has been suggested but not documented in case reports.[17,18] Because the occurrence of AFE bears distinct similarities to anaphylaxis, Clark postulated that high-dose hydrocortisone (500 mg every 6 hours) may be appropriate, but no studies have yet examined this.[5]

Another way of interrupting the natural course of the condition has been considered: Because there is some "toxic" element to the effects of amniotic fluid, a number of reports have suggested that hemofiltration or plasma exchange may be effective in clearing the plasma and aiding recovery. In 1987, a report detailed a successful outcome after 2 exchange transfusions for a probable AFE following amniocentesis.[19] A report in 2001 suggested that transfusing 1.5 times the patient's blood volume acted as an exchange transfusion.[20] When this "cleansing" process was achieved by continuous hemofiltration in 1 case, clotting parameters improved dramatically.[21] This approach may be appropriate after the patient has been stabilized. However, since massive transfusion is a part of initial management when hemorrhage occurs, this may become a treatment by default.

AFE does not make a later successful pregnancy impossible. Six cases have been reported, with good fetal and maternal outcomes.[22-25]

Conclusion

The initial management of AFE is the same as for any collapse—resuscitation and consideration of the diagnosis. One main difference is that other diagnoses must be considered simultaneously and swiftly. If AFE is suspected, aggressive ventilation, inotropic support, and transfusion of volume—including coagulation factors—are required. As yet, no specific therapy exists other than support and transfusion. The condition still leads to significant mortality and morbidity, but milder cases occur and prompt treatment may improve outcome. ■

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