Acute fatty liver of pregnancy: A case report

Acute fatty liver of pregnancy (AFLP) is a potentially fatal metabolic disorder unique to the third trimester of pregnancy. The cause of the disorder remains unknown. It was first identified in 1934 by Sheehan as yellow atrophy of the liver. In 1940, AFLP was identified as an isolated obstetrical emergency. In 1980, the incidence was reported to be as low as 1 per million pregnancies with a subsequent maternal mortality rate of 85%. Numerous case reports since 1980 have elevated the incidence to 1 per 13,328 pregnancies. In 1999, 1 publication reported an incidence of 1 per 6,659 births with no maternal deaths. This increased incidence is related to the recent recognition that this disease manifests itself with a wide range of symptoms and varying degrees of severity. The improvement in maternal morbidity and mortality is credited to early recognition and termination of the pregnancy. This obstetrical emergency can lead to death of both mother and child if not diagnosed in time to prevent coagulopathic complications. This is a case report of an emergency cesarean section in a woman with unrecognized, severe AFLP.

Case report
A 27-year-old woman, gravida 2, para 0, was transferred from a community hospital to the obstetrical unit of a tertiary care center for evaluation of severe preeclampsia at 34 weeks' gestation. Upon arrival, the patient had 2 g of magnesium sulfate infusing intravenously via pump. An additional 16-gauge intravenous line was initiated, and blood was sent to the laboratory for complete blood count, type and screen, and liver enzymes. The patient, though mildly hypertensive, was hemodynamically stable (heart rate, 91 beats per minute; blood pressure, 164/88 mm Hg; respirations, 20 per minute; pulse oximetry, 98% on room air; fetal heart tones, 135 beats per minute). The urine analysis was negative for protein. Dependent edema was noted. The patient was calm and cooperative for her anesthetic interview and revealed that she had no known drug allergies and no medical or surgical history. The patient denied headaches, visual changes, or any bleeding abnormalities. The initial complete blood count showed a hemoglobin level of 13.5 g/dL, a hematocrit of 36.2%, and a platelet count of 214,000/mm³. Liver enzymes were elevated including a total bilirubin of 5.60 µmol/L, a direct bilirubin of 3.4 µmol/L, a lactic dehydrogenase level at 982 U/L, an aspartate aminotransferase of 202 U/L, and an alanine aminotransferase of 332 U/L.

Three hours after admission, the patient was taken to the operating room for an emergency cesarean section secondary to fetal distress. The fetal heart tones had decelerated to 60 to 90 beats per minute for approximately 5 minutes and were unresponsive to maternal position changes and supplemental oxygen by facemask. The patient was premedicated with 30 mL of bicitra orally and 10 mg metoclopramide intravenously. The patient was preoxygenated while standard monitors were applied. Left uterine displacement was maintained. Cricoid pressure was initiated, and general anesthesia was induced with 240 mg of sodium thiopental and 100 mg of succinylcholine intravenously. The patient was preoxygenated while standard monitors were applied. Left uterine displacement was maintained. Cricoid pressure was initiated, and general anesthesia was induced with 240 mg of sodium thiopental and 100 mg of succinylcholine intravenously. A 6.0-mm endotracheal tube was placed. Cricoid pressure was maintained until auscultation of equal bilateral breath sounds and
end-tidal carbon dioxide detection by capnograph verified proper placement. An oral gastric tube was placed to evacuate gastric contents.

Approximately 12 minutes after induction a male infant was delivered and taken to the neonatal intensive care unit. One liter of warmed lactated Ringer solution was initiated with 20 units of pitocin upon delivery of the placenta. The patient was tachycardic, but remained hemodynamically stable (heart rate, 122 beats per minute; blood pressure, 160/75 mm Hg; respirations, 10 per minute; 100% SpO2 on 100% FiO2). The magnesium sulfate infusion was suspected of interfering with the patient’s uterine contraction. Hemabate, 250 μg, was administered via an intrauterine injection. Uterine tone was marginally improved, but hemostasis was not achieved. A 14-gauge angiocath was placed, and a HOTLINE fluid warming set (Level 1, Inc, Rockland, Mass) was used. A forced-air warming blanket was placed over the upper extremities. Additional laboratory tests were ordered including prothrombin time/thromboplastin time, fibrinogen level, and a repeat complete blood count.

The patient's uterine tone remained unsatisfactory and blood loss was now estimated at 1,500 mL. A second dose of hemabate via intrauterine injection and a dose of 0.2 mg of methergine intramuscularly was administered. A nasal temperature probe revealed a body temperature of 34.3°C. A left radial arterial line was placed for arterial blood gas analysis. The first arterial blood gas revealed pH, 7.125; PaCO₂, 43.4; base excess -14; PaO₂, 224; HCO₃⁻, 14; SaO₂, 100% on 50% FiO₂; hemoglobin, 10 g/dL; hematocrit, 30%. An anion gap of 15 is consistent with the metabolic acidosis. Rewarming and continued hemodynamic stability were priorities for improving acidosis. Surgical hemostasis was restored, and the procedure was completed. The patient was then transported to the intensive care unit (ICU) for continued mechanical ventilation and further hemodynamic evaluation. The magnesium sulfate infusion was continued for eclampsia prophylaxis. The patient remained hemodynamically stable during the ICU transport (heart rate, 113 per minute; blood pressure, 134/86 mm Hg; respirations, 10 per minute; 100% SpO₂ on 100% FiO₂). The laboratory data sent intraoperatively confirmed a coagulopathy (prothrombin time, 35.8 seconds; international normalized ratio, 3.3; partial thromboplastin time, 48.2 seconds). Two units fresh frozen plasma were initiated in an attempt to correct this bleeding disorder.

Approximately 4 hours after delivery, a diagnosis of acute fatty liver of pregnancy was made. Despite multiple transfusions of 4 units of packed red blood cells, 4 units of fresh frozen plasma, and 12 units of platelets, the patient remained profoundly coagulopathic (prothrombin time, >100 seconds; international normalized ratio, 10.4; partial thromboplastin time, >132 seconds; hemoglobin, 5.5 g/dL; hematocrit, 17.4%). The patient's temperature was 36.6°C with the assistance of blood warmers and forced air blankets. Her laboratory tests also revealed a coexisting hypoglycemia of 51 mg/dL that was treated with 25 mL of 50% dextrose solution each hour as needed to keep blood glucose levels above 80 mg/dL.

Approximately 10 hours postpartum the patient returned to the operating room for exploration of possible hemorrhage. A large hematoma was evacuated from her abdomen, but no specific source of bleeding was identified. Estimated blood loss from this second procedure was 4,500 mL.

During the first 24 hours postdelivery, the patient received 16 units of packed red blood cells, 17 units of fresh frozen plasma, 30 units of platelets, 3 units of cryoprecipitate, and 2.5 ampules of D50. The patient's coagulopathy was corrected to acceptable levels within a 24-hour period (prothrombin time, 14.9 seconds; international normalized ratio, 1.5; partial thromboplastin time, 40.7 seconds). However, the continued resuscitation had precipitated the onset of adult respiratory distress syndrome. She required increased FiO₂ and positive end-expiratory pressure. Pressure controlled inverse ratio ventilation was employed to maximize oxygenation. These measures, with FiO₂ ranging from 90% to 100%, maintained oxygen saturations of 85% to 90%. The patient's ICU stay was complicated by acute respiratory distress syndrome, septicemia, and renal insufficiency. The patient expired during the sixth postpartum week secondary to complications of adult respiratory distress syndrome.

Discussion

Acute fatty liver of pregnancy is a potentially fatal metabolic disorder unique to the third trimester of pregnancy. The disease is one of a group of microvesicular fat diseases including Reye syndrome, tetracycline toxicity, and hypoglycin toxicity. The exact cause of this disorder is unknown. Grimbert et al found impaired mitochondrial beta oxidation and decreased tricarboxylic acid cycle activity in female mice treated with estradiol and progesterone. These findings suggest that the normal hormonal changes of pregnancy, when combined with other unknown insults, may contribute to the development of AFLP. It is known that AFLP is neither infectious nor inherited. Women who have experienced AFLP rarely suffer this condition with subsequent pregnancies. When AFLP occurs, hepatocytes are infiltrated with free fatty acids.
indicating decreased mitochondrial beta oxidation of medium chain fatty acids and decreased activity of the tricarboxylic acid (Krebs) cycle.\(^7\)\(^8\)

The decline of cellular activity within the hepatocyte is evident by the deterioration in metabolic, synthetic, and excretory functions of the liver.\(^7\) The laboratory data in this case indicated poor hepatic function. Severe cases of AFLP result in hepatic failure with metabolic acidosis, coagulopathy, and hyperglycemia. Metabolic acidosis develops as the damaged hepatocyte becomes unable to clear serum lactate.\(^8\)\(^9\)

An elevated anion gap is present, though this response is muted in light of the patient's hypoaalbuminemia.\(^10\) Correction of metabolic acidosis with sodium bicarbonate remains controversial. The administration of sodium bicarbonate can exacerbate intracellular acidosis through its conversion to carbon dioxide.\(^11\)\(^-13\)

Coagulopathy from reduced clotting factors is the consequence of impaired synthetic function. Depending on the severity of the AFLP, the patient's coagulopathy can range from a mild prolongation of partial thromboplastin time to acute disseminated intravascular coagulopathy. This pathological hepatic condition is usually self-limiting with liver function returning to normal 7 to 9 days after delivery.\(^3\)\(^4\)

The diagnosis of AFLP remains challenging. There is no specific test to identify this condition. The presenting signs and symptoms are varied. This disorder occurs with varying intensity and in conjunction with other third trimester sequelae. Acute fatty liver of pregnancy must be included in the differential diagnosis involving any parturient with abnormal hepatic function. The potentially severe outcome places this disorder on the list with preeclampsia; hemolysis, elevated liver enzymes, and low platelet count (HELLP); viral hepatitis; and hormone-induced cholestasis.\(^3\)\(^-5\) Unfortunately, some signs and symptoms of AFLP are shared with more common disorders of pregnancy including preeclampsia and HELLP syndrome.\(^1\)\(^,4\) Patient outcomes are improved with a high index of suspicion for AFLP. Onset usually occurs at 35 weeks’ gestation. In the prodromal phase, women have nonspecific symptoms including nausea and vomiting, abdominal pain, fever, jaundice, or dark urine.\(^3\)\(^4\) Our patient did not report any prodromal symptoms. Instead, she was admitted for severe preeclampsia with generalized edema and elevated blood pressure (160/75 mm Hg).

The treatment for AFLP is supportive care. Since the exact cause has not been identified, the treatment has not been isolated. Improved maternal outcomes are directly associated with early recognition and prompt termination of the pregnancy. Acute fatty liver of pregnancy commonly occurs after the 35th week of pregnancy, so the newborn usually does well after delivery. A review of reported cases show that none of the patients with AFLP were admitted with that diagnosis. This potentially fatal, uncommon disease should be considered whenever elevated liver enzymes are present after the 30th week of pregnancy. Immediate delivery should be planned for, along with intensive care postdelivery to correct coagulopathy and “supportive care and prevention of extra-hepatic sources of morbidity to allow for recovery from the illness.”\(^4\)

REFERENCES


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